UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/509,449	03/28/2000	KATSUMI AOYAGI	594.352USWO	8016

7590 07/28/2004

MERCHANT & GOULD P.C.
P.O. BOX 2903
MINNEAPOLIS, MN 55402-0903

EXAMINER	
LUCAS, ZACHARIAH	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 07/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/509,449	AOYAGI ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

1. Currently, claims 18-22 are pending and under consideration in the present application. These claims were rejected in the prior action, mailed on September 23, 2003. In the Response filed on March 18, 2003, the Applicant amended claims 18-22.

2. The examiner to whom the case has been docketed in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Examiner Zachariah Lucas in Art Unit 1648.

3. Because this action raises new grounds of rejection, the action is being made Non-Final.

Claim Objections

4. **(Prior Objection- Withdrawn)** Claims 19 and 20 were objected to in the prior action for including language redundant to the claim language in claim 18, the independent claim from which they depend. In view of the cancellation of the language, the objection is withdrawn.

5. **(Prior Objection-Withdrawn)** Claim 20 was objected to in the prior action because the term "antibodies" was misspelled. In view of the amendment to claim correcting the spelling, the objection is withdrawn.

6. **(New Objection)** Claims 19 and 20 are objected to because of the following informalities: it is unclear why the claims refer to both the HCV polyprotein and parenthetically to the HCV core antigen. Because the independent claim from which these claims depend refers only to the core antigen, it is suggested that the same terminology be used in claims 19 and 20: i.e., it is suggested that the dependent claims be amended to refer only to regions of the core antigen. Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. **(Prior Rejection-Withdrawn)** Claims 18-22 were rejected in the prior action under 35 U.S.C. 112, second paragraph, as being indefinite because the claims do not use consistent language. Claim 18 was treated as representative. It was not clear whether each instance of an HCV antigen related to the HCV core antigen. In view of the amendment to the claim clarifying that the HCV antigen is a core antigen, the rejection is withdrawn.

Additionally, claim 19 was rejected because there was no antecedent basis for the term "peptide(s)." In view of the amendment of the claim removing this term from the claims, the rejection is withdrawn.

Additionally, claim 22 was rejected as lacking antecedent basis for the term "the detergent." In view of the amendment of the claim such that the claim now depends from claim 21, which provides antecedent basis for the term, this rejection is also withdrawn.

9. **(New Rejection)** Claims18- 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 18 is treated as representative. This claim described as method "for determining the presence of Hepatitis C virus (HCV) core antigen and/or anti-HCV core antibodies in a sample," but requires in the method the steps to determine the presence of both HCV core antigen and antibodies thereto. It is therefore unclear what is meant by the "and/or" language.

10. **(New Rejection)** Claim 22 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This claim reads on a method for immunoassay for HCV, comprising the use of a detergent with "one or more detergents with one or more alkyl chains of at least 10 carbon atoms and one or more secondary to quaternary amines," and wherein the detergent is a surfactant "with 12 to 16 carbon atoms and a tertiary or quaternary amine." It is not clear if the phrase "with 12 to 16 carbon atoms" is describing the number of carbon atoms in the

Double Patenting

(Prior Rejection-Withdrawn) Claims 21 and 22 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Application No. 10/133,007, now U.S. Patent 6,623,921. In view of the terminal disclaimed filed on March 18, 2004 with respect to the patent, the rejection is withdrawn.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. **(New Rejection)** Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Masalova et al., J Med Virol (of record in the action mailed on September 27, 2001) in view of Papatheodoridis et al. (J Hepatol 24: 36-41), and further in view of the teachings of Ling et al. (GB 2 051 357), and of Schönbrunner (GB 2 313 666). The claim reads on a method for the detection of HCV antigens and antibodies in a sample comprising the use of an antibody against the HCV core protein, and a peptide of an HCV core protein lacking the epitope recognized by the antibody. The method involves the steps of contacting a sample in a vessel with the antibodies and antigens, and detection the formation of immune complexes between HCV antibodies in the sample and the peptide, and between HCV antigens in the sample and the antibody.

Masalova teaches that HCV diagnosis has been based in the past on the detection of antibodies to HCV proteins. The art indicates that antibodies to core protein has been an effective target for such methods. See e.g., Papatheodoridis, page 36. However, Masalova indicates that this method is not sufficient to detect all HCV infections due to the delay in antibody formation upon infection. Page 1. The reference suggests the additional use of methods for the detection of

core antigens in the diagnosis of HCV. Pages 1-2. The reference does not teach the simultaneous detection of both HCV core antigen and antibodies thereto in the same vessel.

However, each of the Ling and Schönbrunner references teach methods for the simultaneous detection of pathogen antigens, and antibodies thereto. Each of these reference indicate that such simultaneous detection of such multiple markers helps to avoid problems relating to the temporal appearance of different markers of the virus after infection, and may be an effective double-check against false-positives. See e.g., Ling, page 1, lines 20-97; and Schönbrunner, pages 2-3, and 4. From these references, it would be obvious to those in the art to apply the double antibody/antigen detection methods applied in these references to the detection and diagnosis of HCV.

It is noted that the present claims require that the peptide used to detect antibodies in the sample to lack the epitope recognized by the antibody used to detect antigen. Such a requirement is obvious in view of the suggestion (e.g.) in the abstract of Ling, indicating that the two different immunoreactants used to detect the antigen and antibody in the sample are "non-complementary" to each other. I.e., the antigen used to detect antibody will not be recognized by the antibody used to detect antigen. Further, the teachings of Schönbrunner on pages 7-8, further indicating that multiple epitopes may be present on any particular antigen, would further indicate that the peptide and antibody used to detect antigen and antibody in the sample may both target different epitopes in the same protein.

The combined teachings of the references therefore render the claimed invention obvious.

13. **(New Rejection)** Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Simmonds et al. (WO 93/10239) in view of Ling and Schönbrunner. Claim 18 has been described above.

Simmonds teaches the use of either HCV core protein antigens or antibodies for the diagnosis of HCV infection. See, pages 5-6. Further, the reference teaches that the detection of HCV through detection of anti-HCV antibodies alone may not be the most reliable means of detecting viral infection, both due to delays in subject seroconversion and to false-positives in immunoassays. Pages 3-4. However, the reference does not teach an assay for detecting both HCV core protein antigens and antibodies in a sample.

However, the teachings of Simmonds in combination with each of Ling and Schönbrunner do suggest such an assay format. The teachings of Ling and Schönbrunner have been described above. As was indicated, the references teach the simultaneous detection of both antigens and antibodies for a pathogen to avoid problems noted by Simmonds with respect to infections by other viruses. Because the Ling and Schönbrunner references suggest such a multi-marker format would overcome the problems noted by Simmonds, it would have been obvious to those in the art to combine the two forms of assay described by Simmonds into an HCV version of the assays described by Ling and Schönbrunner. The combination of the teachings of these three references therefore renders the claimed method obvious.

14. **(New Rejection)** Claims 19 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over either of Masalova and Papatheodoridis, or of Simmonds, in view of Ling and Schönbrunner as applied to claim 18 above, and further in view of either Lacroix (EP 0 507 615)

or Seidel et al. (U.S. Patent 6,183,949). These claims describe the method of claim 18, wherein the antibodies used for detection of HCV core antigen are antibodies that bind to the region comprising residues 100-130 of the HCV core antigen. The teachings of Masalova, Papatheodoridis, Simmonds, Ling, and Schönbrunner have been described above. While the references teach the use of antibodies against the core particle, they do not specify a region of the core particle to be targeted by the antibodies.

However, each of Lacroix and Seidel teach peptide antigens sharing homology to the peptide of SEQ ID NO: 5 of the present application, and that such peptides are useful for the detection of HCV antibodies. See, Lacroix, page 3, SEQ ID NO: 10; and Seidel, col. 1, SEQ ID NO: 22. The references both also teach that antibodies raised against this peptide may similarly be used for the detection of HCV antigens. Lacroix, page 7, lines 41-53; and Seidel, column 6, lines 46-67. The peptide of SEQ ID NO: 5 of the present application is identified as residues 100-120 of the core protein. App., page 22. Because the peptides of Lacroix and Seidel are homologous HCV peptides, they would inherently bind to, or produce, antibodies against peptides comprising the region of residues 100-130 of the core protein. The references therefore suggest the use of such antibodies for the detection of HCV antigens.

Because Lacroix and Seidel suggest the use of such antibodies for the detection of HCV core antigens, and the references cited with respect to claim 18 suggest the use of such antibodies for the detection of HCV, it would have been obvious to those in the art to these antibodies for the detection of HCV core antigens in the methods suggested by the other references. The combined teachings of the references therefore render obvious the use of antibodies directed

against residues 100-130 of the HCV core protein in methods for the simultaneous detection of HCV antigens and antibodies.

15. **(New Rejection)** Claims 21 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over either of Masalova and Papatheodoridis or of Simmonds, in view of Ling and Schönbrunner as applied to claim 18 above, and further in view of either of either Cheng et al. (U.S. 5,627,080) or Khanna et al., (U.S. 5,032,503). These claims describe the method of claim 18, wherein the sample is contacted with the peptide and antibody in the presence of one or more detergents (described above). For the purposes of the present rejection, it is assumed that any detergent comprising 12-16 carbon atoms, and that is a tertiary or quaternary amine meets the claim requirements. It is noted that in the examples of each of Ling and Schönbrunne, detergents are used. However, the references do not appear to teach the use of the claimed class of detergents.

However, each of Cheng and Khanna teach that detergents or surfactants may be used to improve the operation of immunoassays. Cheng, col. 7, lines 26-35; Khanna, col. 2, lines 24-40. As examples of detergents that may be used in the indicated methods, the references respectively indicate that cetyltrimethylammonium bromide, or dodecyltrimethylammonium bromide may be used. Each of these detergents appears to fall within the class of detergents identified in the claims. It would therefore have been obvious to those in the art to use such detergents in the methods suggested by the combination of either Masalova and Papatheodoridis, or Simmonds, with Ling and Schönbrunner as described above.

Conclusion

16. No claims are allowed.

17. The following prior art references are made of record and considered pertinent to applicant's disclosure. However, while relevant they are also not used as a basis for rejection for the stated reasons.

> Each of Dawson et al., U.S. Patent 5,843,450, and O'Connor et al, U.S. Patent 5,627,026 are considered to be close prior art. See e.g., Dawson, columns 16-17, 22-25; and O'Connor, columns 2-4. However, the references do not alone teach or suggest the claimed invention.
>
> Ferroni et al., J Clin Microbiol 31(6): 1586-91. This reference teaches HCV epitopes that overlap with those indicated by the claims.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

JAMES HOUSEL 7/12/04
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600